Remarks

The above Amendments and these Remarks are in reply to the Office Action mailed 17 July 2003. No fee is due for the addition of any new claims. An appropriate Petition for Extension of Time to Respond is submitted herewith, together with the appropriate fee.

Claims 1-11, 31-44 and 110-138 were pending in the Application prior to the outstanding Office Action. In the Office Action, the Examiner rejected all claims. The present Response amends claims 19 and adds new claim 139, leaving for the Examiner's present consideration claims 1-11, 31-44 and 110-139. Reconsideration of the rejections is requested.

I. OBJECTION TO THE ABSTRACT

The Abstract was object to as containing more than 150 words.

The present Response replaces the Abstract with a new one that is shorter than 150 words. Applicants submit that the objection to the Abstract has now been overcome.

II. ART REJECTIONS

The Examiner rejected all pending claims as being unpatentable over a combination of Tu and Clintrial4. Before discussing the rejections, it will be helpful to briefly review what applicants have invented.

As mentioned in great detail in Applicants' specification, at pp. 1-11, the clinical trials industry is huge and highly fragmented among numerous job functions, all the way from study sponsors, to protocol writers, to review boards, to investigators responsible for the overall conduct of an approved trial, to contract research organizations (CROs), to clinicians at the study sites, to data management and analysis companies, to regulatory agency personnel, among many others. Computer support for the industry is also highly fragmented, with many vendors each providing tools for only a small segment of the industry. A list and brief descriptions of some of the major categories of presently available automation tools is provided at pp. 7-10 of Applicants' specification.

Applicants have recognized this fragmentation as a serious problem impeding the efficient development and conduct of clinical trials, and have developed a system that addresses it by, among other things, creating an overall end-to-end system solution which starts with computer-supported protocol authoring assistance and ends with computer support for the conduct of trial by clinical sites, and even reporting back to study sponsors.

In order to support the process from end-to-end, a single protocol modeling database (called an iCP in Applicants' specification) is created to store information related to all supported aspects of the study. This means it might include not only basic study information and study objectives, but also patient eligibility criteria, projected accrual information, and the study schema - a directed graph identifying the various treatment arms of the study, which visits are to take place within each arm and when, what tasks are to be performed in each visit, what branches to take in the workflow in response to particular patient conditions, and so on. In various embodiments of Applicants' invention, all these different kinds of information can be included in the single protocol modeling database.

Prior to Applicants' invention, no vendor offered a system with a protocol modeling database that even came close to covering such diverse aspects of the clinical trials process.

Moreover, according to aspects of the invention, the single database can be used to drive numerous tools specific to each supported aspect of the clinical trial process. The behavior of all these tools is guaranteed to be consistent with each other and with the protocol, because they are all driven by the same protocol modeling database. The behavior of all the tools will also remain consistent with the protocol even as the protocol evolves and changes during the conduct of the study, because the changes can all be incorporated into the same protocol modeling database.

Thus the representation of so many previously diverse aspects of a clinical trial protocol in a single protocol modeling database accomplishes more than just conglomeration. It also enables a level of consistency and data reliability that has not been achievable with the previous fragmented approach.

Applicants submit that their invention is a significant improvement in the art, not obvious over the prior art, and well worthy of a U.S. Patent.

Applicants will now discuss all the rejected claims in sequence.

A. Independent Claim 1

Applicants' claim 1 attempts to capture the comprehensive nature of Applicants' protocol database by focusing on two specific types of information used in aspects of the clinical trial process which in the past have been so widely divergent that no reasonable person of ordinary skill would have considered including both in a single database: patient eligibility criteria and post-enrollment workflow tasks.

Specifically, claim 1 calls for:

> 1. At least one computer readable medium collectively carrying a machine readable database identifying:
>
> first patient eligibility criteria for a first clinical trial protocol; and
>
> a first plurality of workflow tasks for said first clinical trial protocol, said first plurality of workflow tasks including post-enrollment workflow tasks.

Thus claim 1 calls for a machine readable database identifying, among other things, *both* (1) patient eligibility criteria, *and* (2) post-enrollment workflow tasks for the same clinical trial protocol.

Patient eligibility criteria is a *pre*-enrollment concept, useful, for example, in an automated tool to help predict accrual rates, or in an automated tool to help study sites find and qualify patients who might be eligible for a study that has been approved for execution.

Post-enrollment workflow, of course, is a *post*-enrollment concept. As mentioned in Applicants' specification at pp. 11-12, among other places, post-enrollment workflow includes at least two sub-concepts: patient management workflow and post-enrollment data management workflow.

Applicants respectfully submit that claim 1 should be patentable for at least five (5) separate reasons: (1) no reasonable person of ordinary skill would have tried the examiner's

proposed combination; (2) Tu teaches away from combining his system with one like Clintrial4; (3) Clintrial4 also teaches away from a combination with Tu; (4) the Examiner has failed to make a *prima facie* case that there was a motivation to combine the two cited references; and (5) the long-felt, unresolved need in the industry undermines the obviousness of the Examiner's proposed combination.

1. No Reasonable Person of Ordinary Skill Would Have Tried the Examiner's Proposed Combination

In the Office Action, the Examiner rejected claim 1 as being obvious over a combination of Tu and ClinTrial4.

Tu teaches a methodology for automated patient eligibility determination for clinical trials, using a simple language for expressing the *eligibility criteria* of the protocol. The language is translated into queries for use against a database of candidate patient information. The Examiner cited Tu as teaching a database identifying patient eligibility criteria.

As the Examiner points out in the Office action, Tu does not teach or suggest a database that also identifies *workflow tasks* for a clinical trial protocol, and specifically not post-enrollment workflow tasks for a clinical trial protocol.

The Clintrial4 brochure is a product brochure for a Release 4.2 of a product offered by Domain Pharma. As stated on the cover page, Clintrial4 was a "clinical data management" system, and it was cited by the Examiner for teaching a database identifying post-enrollment *workflow tasks*. The Examiner argues that it would have been obvious to combine Tu's database identifying patient eligibility criteria with Clintrial4's database identifying post-enrollment workflow tasks, to make Applicants' claim calling for a database identifying both.

Applicants respectfully disagree. As mentioned, the clinical trials industry, prior to Applicants' invention, was highly splintered into multiple fields of endeavor. Applicants submit that patient eligibility determination and post-enrollment workflow management were in completely different fields, so widely divergent that no reasonable person of ordinary skill would have considered a single database that could support both.

In fact, any workflow identified in the Clintrial4 database was not merely "post-enrollment" workflow; it was specifically *data management* post-enrollment workflow. Its database did not identify any *patient* management workflow tasks at all. It included CRFs and data entry forms to store *data* taken as a *result* of patient management workflow tasks, and included a representation of certain back-end *data* management workflow, but did not identify any *patient* management workflow *tasks*.

The Clintrial4 database was able to store a sequence in which visits were to occur according to the protocol, so that the CRFs in a ClinTrial4 database could be keyed to particular patient visits referred to in the protocol. But even this did not involve identifying in the database patient management workflow *tasks*. There was no sequence of tasks specified *within* a visit, and the system did not use its stored visit sequences to infer any patient workflow.

Thus if one were to think of the execution of a clinical trail as having three main segments - pre-enrollment activities, post enrollment *patient* related activities, and *data* management activities undertaken in response to certain of the patient related activities, Tu would be limited to the first of these segments and Clintrial4 would be limited to the third of these segments. Neither reference addresses the second of these segments, the broad middle of the execution of the trial.

In fact, the clinical trials industry is actually divided into many more than three "silos of responsibility". The silos are very narrow, because people of ordinary skill in each silo are narrowly focused on their specific narrow responsibilities in the overall process. The silos are very tall, because each field requires great depth of knowledge in order to discharge the responsibilities of the field safely and competently. While different companies can make various different categorizations, the following exemplary division of responsibilities will give the Examiner more of a feel for just how diverse these "silos" are:

Role/Responsible person	Type of workflow tasks of concern
Medical Monitor (physician)	Clinical tests which measure disease and treatment response
Regulatory Monitor	Safety tests which meet regulatory concerns
Statistician	Measurements that are sensitive enough to show statistically significant differences
Clinical Ops team leader	Identification of tasks to be done at local trial site versus central site (e.g. which tests are to be made by local site versus being sent out to a central lab for processing instead). Workflow tasks associated with getting a site up and running: -- Required FDA documents filed? (Form 1572) -- Site preparation visit completed? -- Local IRB approved the informed consent? -- Investigator contract signed?
Clinical Monitor	Have all the required tests been done within the specified time window? This person does not care about values, just done/not-done on time.
Clinical Data Manager	Are all the data forms complete? Do the data values pass validation (are they believable)? If not, need to get clarification regarding unbelievable values

In this more representative example of the numerous "silos of responsibility" which fragment the clinical trials industry, a user of Tu's system might be in the Medical Monitor silo, whereas a user of Clintrial4 would be in the Clinical Data Manager silo -- which is not two, but 5 distinct fields distant from the user of Tu's system. Vendors of technology to assist workers in the industry are also focused within narrow silos matching those of their customers.

Under these circumstances, Applicants' respectfully submit that the two art fields to which Tu and Clintrial4 were directed were so far apart that no reasonable person of ordinary skill would have found it obvious to combine them. In the deeply fragmented clinical trials industry, a reasonable person focused on automating pre-enrollment activities, such as Tu's patient eligibility criteria, would simply have not tried to incorporated workflow tasks as far downstream in the process as Clintrial4's data management workflow, and vice-versa. Moreover,

as discussed more fully below, both references actually teach away from such a combination, there was no motivation to combine them, and the long-felt, unresolved need for the claimed combination objectively confirms its unobviousness.

2. Tu Teaches Away from Combining His System with One like Clintrial4

Tu teaches a motivation for not combining his eligibility determination system with systems addressing other, downstream, "silos" in the execution of a clinical trial. Because the clinical trials industry is so huge and includes so many disparate aspects, people of ordinary skill developing technology to assist in one segment of the industry are reluctant to involve themselves in another segment because of insufficient expertise in the second segment. It is perhaps for this reason that Tu, in discussing the promise of his eligibility determination system, says:

> Unlike diagnostic programs that require extensive knowledge about diseases and their possible signs and symptoms, the domain knowledge required by eligibility-determination systems is constrained by the eligibility criteria of clinical-trial protocols. (Tu, p. 14, lines 4-7) (emphasis added).

In other words, whereas his system is workable for representing an aspect as simple as eligibility criteria, it may not be workable for representing diagnostics because of the much more extensive "domain knowledge" that would be required.

This language in Tu therefore suggests not expanding his system to diagnostic realms.

Workflow management for the conduct of a clinical trial protocol is much the same in this sense as diagnostic realms----it requires much more extensive knowledge about disease signs and symptoms than does patient eligibility determination. *Data* management workflow is also much more complicated than patient eligibility determination, because of the need to understand statistics and the exacting data handling requirements imposed by regulatory agencies.

Thus effectively, Tu teaches away from the combination of his system with a system addressing data management workflow tasks like Clintrial4.

Accordingly, Applicants respectfully submit that not only were the fields of Tu and Clintrial4 too far apart for reasonable practitioners to have considered combining them, but Tu effectively teaches away from such a combination.

Applicants therefore submit that claim 1 should be patentable for this reason as well.

3. Clintrial4 Also Teaches Away from a Combination with Tu

The Clintrial4 brochure, too, teaches a motivation for not combining with Tu. Page 1 of the brochure (the front page) contains the following language:

> DOMAIN
>
> Proven Clinical and Regulatory Solutions
>
> Domain Pharma Corporation is the world's leading provider of proven clinical and regulatory solutions. The company's software and services enables pharmaceutical and biotechnology companies to optimize the processes they use for clinical data management and adverse event tracking. These products and services address the entire continuum of clinical research from data capture and management to medical data review and safety reporting. Domain Pharma's focus, stability, technological innovation and customer commitment has enabled the company to maintain successful relationships with leading pharmaceutical, biotechnology, contract research and medical device organizations around the world. (emphasis added)

As can be seen, the focus of Domain Pharma is entirely in the segment of *data* management, and activities even further downstream from data capture. Though the language refers to this segment as an "entire continuum of clinical research", this company's view of the "entire continuum" does not encompass the more upstream segment of *patient* management workflow, and certainly not the even more upstream segment of *pre*-enrollment activities, such as Tu.

Importantly, the company promotes itself on the ground that it is "focus[ed]" within that segment of the clinical trials process. By boasting that it is "focused" in that segment, the brochure implies that expansion into other segments would be a detriment, not an advantage.

This sentiment is consistent, once again, with the notion described above that each "silo of responsibility" in the clinical trials process requires so much in-depth knowledge unique to that segment, that people of ordinary skill in one such segment would have been reluctant to expand into another such segment.

Accordingly, not only were the fields of Tu and Clintrial4 too far apart for reasonable practitioners to have considered combining them, but the Clintrial4 brochure, like Tu, effectively teaches away from the proposed combination.

4. There Was No Motivation to Combine the Two Cited References

As is well established, when asserting that a combination of references would have been obvious, the Examiner is required to set out explicitly, based on objective evidence of record and not merely common knowledge or common sense, why a person of ordinary skill would have been motivated to combine the cited references. As forcefully stated in *In re Lee*, 277 F.3d 1338, 61 U.S.P.Q.2D 1430 (Fed. Cir. 2002):

> The factual inquiry whether to combine references must be thorough and searching." (Citations omitted.) It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with.
> ...
> The need for specificity pervades this authority. See, e.g., In re Kotzab, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000) ("particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed"); In re Rouffet, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) ("even when the level of skill in the art is high, the Board must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination. In other words, the Board must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious."); In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (the examiner can satisfy the burden of showing

> obviousness of the combination "only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references"). (emphasis added).

In the face of the exacting requirements imposed by the Federal Circuit, in the Office action, the Examiner says merely that a person of ordinary skill would have made the Examiner's proposed combination "for the motivation of a product that delivers clean accurate data while ensuring regulatory compliance." The Examiner cites p.1 of the Clintrial4 brochure for this motivation. There are at least two problems with the motivation stated by the Examiner.

First, the actual quote from the Clintrial4 brochure is that "A clinical data management system (CDMS) that delivers clean, accurate data can also help you maintain regulatory compliance...." The language might motivate one to improve a clinical data management system, but provides no motivation whatsoever to combine a clinical data management system with a system so far upstream in the clinical trial process as Tu's pre-enrollment patient eligibility criteria.

Second, the motivation stated by the Examiner would in no way motivate the person of ordinary skill to combine the teachings of the *two specific* references cited by the Examiner, as required by the Federal Circuit.

-- What is it about this motivation that would cause the person to select Tu to combine with Clintrial4?

-- The language referenced by the Examiner focuses on the post-enrollment data management segment of the clinical trial process, so what is it about the language that would have motivated a person to focus on eligibility criteria, at least two major segments upstream of the data management segment?

-- What is it about this motivation that would cause the person to identify both Tu's information and Clintrial4's information in a common database (rather than, for example, separate databases from different vendors, operated sequentially by different personnel, as in the previous world of clinical trials)?

Since the Examiner has answered none of these questions, Applicants respectfully submit that the Examiner has failed to make a *prima facie* case of obviousness because he has not yet made a *prima facie* case that a person of ordinary skill would have been motivated to make the specific combination of Tu and Clintrial4. The motivation stated by the Examiner is not "thorough and searching", nor does it explain why the person of ordinary skill "would have been motivated to select the references and to combine them".

5. The Long-felt, Unresolved Need in the Industry Undermines the Obviousness of the Examiner's Proposed Combination

The motivation identified by the Examiner in the Office action–delivering clean, accurate data while ensuring regulatory compliance--- far from supporting the obviousness of the Examiner's combination, in fact supports the *un*obviousness of Applicants' invention. The kind of desire identified by the Examiner has existed for many, many years without anyone having made the combination. See, for example, the lengthy description in the Background section of Applicants' specification at pp. 1-11, describing the sad state of affairs in clinical trials methodology prior to Applicants' invention. The Examiner is respectfully referred to that description so that it need not be repeated here.

Applicants respectfully submit that the need identified by the Examiner *did* exist, and has been extremely long-felt. Yet the need has gone unresolved for many years prior to Applicants' invention.

Thus Applicants respectfully submit that even if the Examiner were able to find a motivation in the art for combining Clintrial4 and Tu, claim 1 nevertheless *still* should be patentable because it solves a long-felt, unresolved need in the industry for a more comprehensive clinical trials management system that can be used to "deliver clean accurate data while ensuring regulatory compliance".

Accordingly, claim 1 should be patentable.

B. Dependent claims 2-11

Claims 2-11 all depend ultimately from independent claim 1 and should therefore be patentable for at least the reasons set forth above with respect to claim 1. These claims also add their own limitations which, it is submitted, render them patentable in their own right.

For example, without limitation, **claim 5** adds a limitation that the post-enrollment workflow tasks called for in claim 1 specifically include *patient* management tasks. As explained above with respect to claim 1, neither Tu nor Clintrial4 include a database identifying *patient* management tasks.

The Examiner points to two sections of the Clintrial4 brochure which he asserts teach that the Clintrial4 database identify *patient* management tasks: the section entitled Clintrial Admin and the section entitled Clintrial Enter.

The Clintrial Admin section of the brochure describes a module in Clintrial4 used to assign security to *data* taken from patients during the conduct of the trial. The description says that the module enables system administrators to assign, monitor and control access to sensitive "clinical *data* records." Clinical *data* records are the records of data resulting from patient tests, not any representation of *tasks* defined as part of the overall protocol.

The description in the brochure of the "Clintrial Enter" module of the product says that it allows a user to "interact with clinical records based on predefined study books, or using custom-built navigation pathways." But "study books" are nothing more than collections of CRF data screens, analogous to collections of printed CRF pages. Navigation pathways are nothing more that sequences that will be followed by the system as the user navigates through the CRF data screens while entering or reviewing data. Again, this is data management, and says nothing about patient management workflow tasks.

The brochure's description of the "Clintrial Enter" module continues, saying that it allows a user to "see an overview of subjects, visits and CRF pages that have associated data collections. Annotations indicating specific entry issues can be added to CRF pages...." Again this focus on CRF pages emphasizes the clinical *data* management function of the ClinTrial4 database, as opposed to any representation of workflow *tasks* to be performed during the conduct of a trial.

Accordingly, Applicants submit that the Examiner is mistaken to cite the Clintrial4 brochure as teaching that the Clintrial4 database identified *patient* management tasks. And since neither Tu nor Clintrial4 teach a database identifying *patient* management tasks, neither reference of the Examiner's proposed combination teaches an element called for in claim 5. Claim 5 therefore should be patentable for this reason as well.

As another example, **claim 6** adds a limitation that the post-enrollment workflow tasks called for in claim 1 specifically include the *data* management task of instructing "a clinician to complete a specified form." More specifically, Claim 6's grandparent claim 1 calls for a database identifying certain workflow *tasks*, and intervening claim 4 adds a limitation that the tasks identified in the database include *data* management tasks. Claim 6 then adds a further limitation that at least one of the data management tasks identified in the database include an instruction for a clinician to complete a specified form.

The Examiner cites "automated eligibility determination" at pp. 2-3 of Tu as teaching this limitation, but nothing about Tu's "automated eligibility determination" suggests a *database* identifying the workflow *task* of *instructing* a clinician to complete a specified form. This claim calls for more than the existence of a form that the clinician can complete.

It may be that the Examiner is reading Tu's Fig. 2 as teaching such an instruction in such a database. But this diagram does not purport to illustrate a workflow graph identified in a machine readable database. Rather, this diagram illustrates the author's understanding of how a clinician, prior to Tu's paper, typically went about identifying patients eligible for a clinical trial. (Tu, p.1, lines 37-38).

Accordingly, Applicants submit that the Examiner has not made a *prima facie* case that claim 6 is unpatentable, since he has not cited a reference to teach that the database include an instruction for a clinician to complete a specified form.

As yet another example, **claim 7** adds a limitation that the post-enrollment workflow tasks called for in claim 1 specifically include "an instruction for a clinician to obtain informed consent of a patient." The Examiner cites Tu's Fig. 2 as teaching this limitation, but again, Tu's Fig. 2 does not purport to illustrate tasks identified in a machine readable database. It is only a

representation of how Tu believes a clinician, prior to Tu's paper, typically went about identifying patients eligible for a clinical trial. (Tu, p.1, lines 37-38). In fact, nothing in Tu teaches or makes any suggestion that a *machine readable database* include "an instruction for a clinician to obtain informed consent of a patient," as called for in claim 7.

Accordingly, Applicants submit that the Examiner has not made a *prima facie* case that claim 7 is unpatentable.

Claims 8-9 each depend ultimately from claim 7, which as just explained, should be patentable.

As yet other examples, **claims 10 and 11** each add a limitation that a data management task identified in the machine readable database "include an instruction to enroll a patient into a clinical trial." Again the Examiner cites Tu's Fig. 2 as teaching this limitation, but again, Tu's Fig. 2 does not purport to illustrate tasks identified in a machine readable database. Tu in fact neither teaches nor suggests that a *machine readable database* include an *instruction* to "enroll a patient into a clinical trial."

Accordingly, Applicants submit that the Examiner has not made a *prima facie* case that claims 10 and 11 are unpatentable.

Accordingly, since the Examiner has not made a *prima facie* case that dependent claims 2-11 are unpatentable, Applicants submit that these claims should be allowable.

C. Independent Claim 31

The Examiner rejected claim 31 over the same combination of Tu and the ClinTrial4 brochure.

As amended in the present Response, claim 31 calls for, among other things, a computer readable medium collectively carrying:

> a library identifying a plurality of machine readable protocol databases each identifying, for a respective clinical trial protocol, at least one member of the group consisting of patient eligibility criteria and patient management protocol workflow tasks. (emphasis added).

The Examiner cites Tu as teaching a database identifying, for *one* clinical trial protocol, one member of the claimed group (specifically the first member of the claimed group, patient eligibility criteria). But the Examiner notes that Tu does not teach or suggest a *library* identifying a *plurality* of protocol databases each identifying a member of the group.

To remedy this deficiency, the Examiner again cites the ClinTrial4 Rel 4.2 brochure. However, to the extent Clintrial4 or the brochure included workflow tasks, they were only data management workflow tasks, not patient management workflow tasks. See the discussion above with respect to claim 1 for an explanation of why Clintrial4 and the brochure included only data management workflow tasks. Data management workflow tasks are not in the claimed group, and represent a completely different segment of the clinical trial process from those that *are* in the claimed group.

Since Clintrial4 was limited to data management, the Examiner's rejection reduces to a combination of two references, one of which (Tu) teaches a database identifying a member of claim 31's group for only *one protocol*, and the other of which (Clintrial4) teaches a *library* of protocols generally. The Examiner's position is that it would have been obvious to combine Tu and Clintrial4 to arrive at a *library* of protocol databases each identifying a member of claim 31's group.

The Examiner has not made a *prima facie* case that it would have been obvious to combine these two references in the manner of Applicants' claim 31. All five reasons set forth above with respect to claim 1 apply here as well. In particular: (1) no reasonable person would have tried the examiner's proposed combination; (2) Tu teaches away from combining his system with one like Clintrial4; (3) Clintrial4 also teaches away from a combination with Tu; (4) the Examiner has failed to make a *prima facie* case that there was a motivation to combine the two cited references; and (5) the long-felt, unresolved need in the industry undermines the obviousness of the Examiner's proposed combination.

Accordingly, claim 31 is believed to be patentable.

D. Dependent Claims 32-44

Claims 32-44 all depend ultimately from independent claim 31 and should therefore be patentable for at least the reasons set forth above with respect to claim 31. These claims also add their own limitations which, it is submitted, render them patentable in their own right.

For example, without limitation, **claim 34** depends from claim 31 and adds limitations similar to those of independent claim 1. Claim 34 therefore should be patentable for all the reasons that claim 1 is patentable, in addition to those for which claim 31 is patentable.

As another example, **claim 36** depends from claim 31 and adds limitations that the post-enrollment workflow tasks identified in the database specifically include both data management tasks *and patient* management tasks. As explained above with respect to claims 1 and 5, neither Tu nor Clintrial4 include a database identifying *patient* management tasks.

As other examples, **claims 41-44** add limitations calling for specific kinds of object classifications, dependent upon differing clinical trial protocols and differing disease categories. The Examiner takes official notice "that it was well known" to use "object oriented programming", but does not take official notice (nor could he) of the specific kinds of object classifications recited in these claims. Nor does he cite any reference teaching such object classifications.

Since the Examiner has not cited any reference teaching the limitations called for in these claims, even the combination proposed by the Examiner cannot teach such limitations. The Examiner therefore has failed to make a *prima facie* case that these claims are unpatentable.

Accordingly, Applicants submit that dependent claims 32-44 should be allowable.

E. Independent Claim 110

The Examiner rejected claim 110 over the same combination of Tu and the ClinTrial4 brochure.

As amended in the present Response, Claim 110 calls for, among other things, a clinical trials method, comprising the steps of:

storing in a library of clinical trial sub-protocol components, a first clinical trial sub-protocol component identifying at least one member of the group consisting of a patient eligibility criterion and a patient management protocol workflow task; and

assigning a first sub-protocol component level user access control to said first clinical trial sub-protocol component in said library.

The Examiner cites Tu as teaching a library of clinical trial sub-protocol components, including one identifying a patient eligibility criterion, but notes that Tu does not teach or suggest assigning sub-protocol component level user access controls to the clinical trial sub-protocol component in the library.

To remedy this deficiency, the Examiner again cites the ClinTrial4 Rel 4.2 brochure.

Again, however, Clintrial4 teaches neither a patient eligibility criterion nor a *patient* management workflow task. Thus the Examiner's position reduces to the combination of Tu, for teaching a sub-protocol component (specifically a patient eligibility criterion), but *not* a library of sub-protocol components and *not* sub-protocol component level user access controls; and the Clintrial4 brochure for teaching certain fine grain user access control, but not of one of the claimed sub-protocol components. As explained above, Clintrial4 does not even include either of the claimed sub-protocol components anywhere in its database.

For the reasons set forth above with respect to claims 1 and 31, Applicants submit that the Examiner has not made a *prima facie* case that it would have been obvious to combine these two references in the manner of Applicants' claim 110. Again, all five reasons set forth above with respect to claim 1 apply here as well. In particular: (1) no reasonable person would have tried the examiner's proposed combination; (2) Tu teaches away from combining his system with one like Clintrial4; (3) Clintrial4 also teaches away from a combination with Tu; (4) the Examiner has failed to make a *prima facie* case that there was a motivation to combine the two cited references; and (5) the long-felt, unresolved need in the industry undermines the obviousness of the Examiner's proposed combination.

Accordingly, claim 110 is believed to be patentable.

F. Dependent Claims 111-119

Claims 111-119 all depend ultimately from independent claim 110 and should therefore be patentable for at least the reasons set forth above with respect to claim 110. These claims also add their own limitations which, it is submitted, render them patentable in their own right.

For example, without limitation, **claim 111**, as amended, adds limitations similar to those of independent claim 31. Claim 111 therefore should be patentable for all the reasons set forth above with respect to claim 31, in addition to those for which claim 110 is patentable.

Accordingly, Applicants submit that dependent claims 111-119 should be allowable.

G. Independent Claim 120

The Examiner rejected claim 120 over the same combination of Tu and the ClinTrial4 brochure.

As amended in the present Response, Claim 120 calls for, among other things, a clinical trials method, comprising the steps of:

> storing a plurality of clinical trial sub-protocol components each identifying at least one member of the group consisting of a patient eligibility criterion and a *patient management* protocol workflow task; and
>
> providing access to individual ones of said clinical trial sub-protocol components by each of a plurality of users in accordance with predetermined sub-protocol component level access controls. (emphasis added)

The Examiner cites Tu as teaching a plurality of clinical trial sub-protocol components, including one identifying a patient eligibility criterion, but notes that Tu does not teach or suggest assigning sub-protocol component level user access controls to the clinical trial sub-protocol component in the library.

To remedy this deficiency, the Examiner again cites the ClinTrial4 Rel 4.2 brochure.

Again, however, as set forth above with respect to claim 110, Clintrial4 teaches neither a patient eligibility criterion nor a *patient* management workflow task. Thus the Examiner's position reduces to the combination of Tu, for teaching a sub-protocol component (specifically a

patient eligibility criterion), but *not* a library of sub-protocol components and *not* sub-protocol component level user access controls; and the Clintrial4 brochure for teaching certain fine grain user access control, but not of one of the claimed sub-protocol components.

For the reasons set forth above with respect to claims 1, 31 and 110, Applicants submit that the Examiner has not made a *prima facie* case that it would have been obvious to combine these two references in the manner of Applicants' claim 120. Again, all five reasons set forth above with respect to claim 1 apply here as well. In particular: (1) no reasonable person would have tried the examiner's proposed combination; (2) Tu teaches away from combining his system with one like Clintrial4; (3) Clintrial4 also teaches away from a combination with Tu; (4) the Examiner has failed to make a *prima facie* case that there was a motivation to combine the two cited references; and (5) the long-felt, unresolved need in the industry undermines the obviousness of the Examiner's proposed combination.

Accordingly, claim 120 is believed to be patentable.

H. Dependent Claims 121-127

Claims 121-127 all depend ultimately from independent claim 120 and should therefore be patentable for at least the reasons set forth above with respect to claim 120. These claims also add their own limitations which, it is submitted, render them patentable in their own right.

For example, without limitation, **claim 121**, as amended, adds limitations similar to those of independent claim 31. Claim 121 therefore should be patentable for all the reasons set forth above with respect to claim 31, in addition to those for which claim 120 is patentable.

Accordingly, Applicants submit that dependent claims 121-127 should be allowable.

I. Independent Claim 128

The Examiner rejected claim 128 over the same combination of Tu and the ClinTrial4 brochure.

As amended in the present Response, Claim 128 calls for, among other things, a computer readable medium carrying:

a library identifying a plurality of clinical trial sub-protocol components each identifying at least one member of the group consisting of patient eligibility criteria and protocol workflow tasks, said library further identifying sub-protocol component level user access controls for at least a subset of said sub-protocol components. (emphasis added)

The Examiner again cites Tu as teaching a plurality of clinical trial sub-protocol components, including one identifying a patient eligibility criterion, but notes that Tu does not teach or suggest assigning sub-protocol component level user access controls to the clinical trial sub-protocol component in the library. Again to remedy this deficiency, the Examiner cites the ClinTrial4 Rel 4.2 brochure.

Again, however, as set forth above with respect to claims 110 and 120, Clintrial4 teaches neither a patient eligibility criterion nor a *patient* management workflow task. Thus the Examiner's position reduces to the combination of Tu, for teaching a sub-protocol component (specifically a patient eligibility criterion), but *not* a library of sub-protocol components and *not* sub-protocol component level user access controls; and the Clintrial4 brochure for teaching certain fine grain user access control, but not of one of the claimed sub-protocol components.

For the reasons set forth above with respect to the other independent claims, Applicants submit that the Examiner has not made a *prima facie* case that it would have been obvious to combine these two references in the manner of Applicants' claim 128. Again, all five reasons set forth above with respect to claim 1 apply here as well. In particular: (1) no reasonable person would have tried the examiner's proposed combination; (2) Tu teaches away from combining his system with one like Clintrial4; (3) Clintrial4 also teaches away from a combination with Tu; (4) the Examiner has failed to make a *prima facie* case that there was a motivation to combine the two cited references; and (5) the long-felt, unresolved need in the industry undermines the obviousness of the Examiner's proposed combination.

Accordingly, claim 128 is believed to be patentable.

J. Dependent Claims 129-138

Claims 129-138 all depend ultimately from independent claim 128 and should therefore be patentable for at least the reasons set forth above with respect to claim 128. These claims also add their own limitations which, it is submitted, render them patentable in their own right.

For example, without limitation, **claim 129**, as amended, adds limitations similar to those of independent claim 31. Claim 121 therefore should be patentable for all the reasons set forth above with respect to claim 31, in addition to those for which claim 128 is patentable.

Accordingly, Applicants submit that dependent claims 129-138 should be allowable.

Conclusion

The amendments to the claims not referenced above are made to correct typographical errors.

New dependent claim 139 has been added to more particularly point out the invention.

The references cited by the Examiner but not relied upon have been reviewed, but are not believed to render the claims unpatentable, either singly or in combination.

In light of the above, it is respectfully submitted that all of the claims now pending in the subject patent application should be allowable, since the Examiner has failed to make a *prima facie* case of unpatentability. A Notice of Allowance is therefore requested. The Examiner is respectfully requested to telephone the undersigned if he can assist in any way in expediting issuance of a patent.

Enclosed is a PETITION FOR EXTENSION OF TIME UNDER 37 C.F.R. § 1.136 for extending the time to respond up to and including 17 December 2003.

Also enclosed is a Third Information Disclosure Statement.

The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 50-0869 for any matter in connection with this response, including any fee for extension of time, which may be required.

Respectfully submitted,

Date: 12/17/2003

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